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PATENT
Docket No. 506562000200

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Chase Trombella

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Warren HOEFFLER

Serial No.: 09/622,703

Filing Date: August 21, 2000

For: METHOD FOR DETERMINING TRANSCRIPTION FACTOR ACTIVITY AND ITS TECHNICAL USES

Examiner: A. K. Chakrabarti

Group Art Unit: 1634

REPLY UNDER 37 CFR §1.116 -- EXPEDITED PROCEDURE -- EXAMINING GROUP 1634

Do not Enter
Arun Kr. Chakrabarti

Box AF
Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

This is in response to the final Office Action dated June 6, 2002 for which a response is due by September 6, 2002.

REMARKS

Claims 1-14 are pending. All pending claims are believed to be in condition for allowance, as is further established by the accompanying remarks. Withdrawal of the finality of the Office Action and reconsideration is respectfully requested.

Claim Rejections - 35 U.S.C. § 102(b)

The Examiner has rejected claims 1-2, 4-8, and 10-13 under 35 U.S.C. § 102(b) as being anticipated by Gansz, et al. (Molecular and General Genetics, (1991), Vol. 225, 427-434). Applicant traverses the rejection.

As further addressed below, the inherent properties of the bacterial phage (virus) binding protein DsbA disclosed by Gansz, et al. cannot anticipate Applicant's claimed methods, nor does Gansz, et al. otherwise, either explicitly or implicitly, teach or suggest the claimed methods.

The Claimed Invention

The presently claimed invention is drawn to methods of detecting transcription activity, wherein the presence of a nick in a DNA molecule is indicative of transcription activity. As set forth in the sepcification, the nick in the DNA serves as an entry site for an RNA polymerase complex. The complex migrates down the DNA to the transcription start site where transcription is initiated.

For convenience, independent claims 1 and 10 are reproduced below:

> 1. A method of detecting transcription activity comprising detecting the presence or absence of a nick in a DNA molecule, wherein the presence of a nick in the DNA molecule indicates transcription activity.

10. A method of detecting transcription activity comprising the steps of :
a) providing a DNA template comprising at least one binding region for a transcription factor;
b) contacting the DNA template with at least one transcription factor; and
c) detecting the presence or absence of a nick in the DNA template, wherein the presence of a nick in the DNA template indicates transcription activity.

Dependent claims from claims 1 or 10 above include methods wherein the nick is detected by an electrophoretic gel, primer extension reaction, PCR amplification reaction, DNA sequencing assay, and protein binding assay. Additional dependent claims from claims 1 or 10 are directed to methods wherein the DNA is affixed to a gel matrix, the transcription factor is in a nuclear cell extract, and the DNA template is inserted into a viral or plasmid vector and introduced into a cell.

The Prior Art

Gansz, et al. disclose a specific bacterial phage (virus) binding protein, DsbA, that binds late transcription promoters, and which also nicks DNA. Of critical importance in the present case, and as further discussed herein, Gansz, et al. makes no mention whatsoever of methods of detecting transcription activity that rely upon detection of such nicked DNA, as is claimed.

The Examiner's Argument

In sustaining the rejection, the Examiner alleges the following:

> Gansz et al teach a method of detecting transcription activity (Summary) comprising the steps of:
> a) providing a DNA template comprising at least one binding region for a transcription factor (Page 428, column 1, Materials and Methods Section, DNA isolation subsection);
> b) contacting the DNA template with at least one transcription factor (Figures 1 and 2 and Materials and Methods Section, Gel-retardation assay subsection);

c) detecting the presence or absence of a nick in the DNA template, wherein the presence of a nick in the DNA template indicates transcription activity (Summary, lines 11-12 and Results and Discussion section, The DsbA protein induces DNA nicking subsection and Figures 2-5).

Gansz et al teach a method wherein the presence or absence of a nick in a DNA molecule is measured by determining the change in electrophoretic mobility of nicked DNA on an electrophoretic gel by a DNA sequencing assay (Figure 5 and Materials and Methods Section, DNAse I foot printing subsection).

Gansz et al teach a method wherein the presence or absence of a nick in a DNA molecule is determined by a primer extension, polymerase chain reaction and amplification reaction (Materials and Methods Section, DNA sequencing subsection).

Gansz et al teach a method wherein the presence or absence of a nick in a DNA molecule is determined by a protein binding assay (Figure 2 and Results and Discussion section, Gel Retardation Assay subsection).

Gansz et al teach a method wherein the DNA is affixed to a gel matrix (Figures 2-5 and Materials and Methods Section, In vitro transcription assays subsection).

(Office Action, pages 2-3.) Applicant disagrees with this characterization of Gansz, et al. As previously argued in Applicant's prior filed response of April 5, 2002 and as further discussed herein, Gansz, et al. cannot be relied upon for teaching or suggesting the claimed methods of detecting transcription activity that rely upon detection of nicked DNA.

Gansz, et al., discloses a specific bacterial phage (virus) binding protein, DsbA, and teaches that the DsbA binding protein nicks DNA. That is all. But Applicant is not attempting to claim a phage binding protein that nicks DNA. Instead, the claimed invention is directed to methods of detecting transcription activity that rely upon detection of nicked DNA. Any suggestion that these claimed methods can somehow be extracted from the teachings of Gansz, et al. is simply unfounded.

Furthermore, at page 7 of the Office Action, the Examiner appears to support the rejection of the claimed methods on the basis of inherent properties of the DsbA binding protein (a compound). Specifically, the Examiner states "the property of transcription as a result of nicking is inherently present in this chemically and structurally identical molecule." But, and as further discussed herein, the inherent properties of a compound alone are not sufficient to render method claims unpatentable. Thus any such rationale for supporting the rejection is misplaced.

Inherent properties of DsbA binding protein do not render claimed methods unpatentable

A prior art reference can anticipate a claim without expressly disclosing each and every limitation of the claim, provided those claim limitations not expressly disclosed are otherwise inherently found within the reference. *See e.g., Atlas Powder Co. v. Ireco, Inc.*, 190 F.3d 1342, 51 USPQ2d 1943 (Fed. Cir. 1999), *Continential Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 20 USPQ2d 1746 (Fed. Cir. 1991). It is well settled that the discovery of a previously unknown advantage of a known compound does not render the compound itself patentable anew. *Titaniumn Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985). It is equally well settled that discovering and claiming a new benefit of an old process likewise cannot render the process again patentable. *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). However, it has never been the case that a known compound per se renders new methods of use unpatentable. *See In re Woodruff*, 919 F.2d at 1578, 16 USPQ2d at 1936 (citing cases where inventions to a new use of an old or obvious compound were held patentable). Rather, inherency requires a determination of whether the inherent characteristic relied upon is necessarily present in what is described in the relied upon reference, and whether it would be so

recognized by persons of ordinary skill in the art. *Continental Can*, 948 F.2d at 1268, 20 USPQ2d at 1749.

In the present case, the Gansz, et al. reference fails on this account. At most, Gansz, et al. teaches a transcription factor DbsA that nicks DNA. But Gansz, et al. does not teach methods of detecting transcription activity that rely upon detecting the presence of nicked DNA, as is claimed. Further, Gansz, et al. in no way appreciates that nicking of DNA is predictive of transcription activity, therefore Gansz, et al. cannot be relied upon for even suggesting the claimed methods.

Gansz, et al., cannot be relied upon for teaching claimed methods

Turning now to the reference itself, Applicant has already provided ample and sufficient arguments as to why the Examiner's interpretation of what Gansz, et al. teaches is mistaken. (See Applicant's prior response.) For the sake of brevity, Applicant reaffirms the positions set forth in Applicant's prior response, with particular attention to the following.

On page 2 of the Office Action, the Examiner asserts:

> Gansz, et al. teach a method of detecting transcription activity (Summary) comprising the steps of a) . . .b) . . . and, c) detecting the presence or absence of a nick in the DNA template, wherein the presence of a nick in the DNA template indicates transcription activity (Summary, lines 11-12 and Results and Discussion section, The DsbA protein induces DNA nicking subsection and Figures 2-5).

As previously pointed out by Applicant, Gansz, et al. fails to appreciate, explicitly or otherwise, that the presence or absence of a nick is predictive of transcription. In particular, none of the specific citations cited by the Examiner (i.e., Summary, lines 11-12 and Results and Discussion section, The DsbA protein induces DNA nicking subsection and Figures 2-5), either

explicitly or implicitly, point to assaying for transcription activity by identifying the presence of a nick in the DNA. Again, Gansz, et al. teach a gene product that binds, and separately causes nicks in, a double stranded DNA molecule, but any similarity to the claimed invention ends there.

This lack of explicit or implicit teaching of the claimed methods is buttressed by Gansz, et al.'s lack of understanding as to the role of the DNA nicking produced by the DsbA protein. In fact, Gansz, et al. find their functional assay results inconclusive as to the role of the observed nicking. Gansz, et al. state that that "surprisingly, the nicks occur on the template strand and must separate the promoter from downstream structural genes," for which the authors explicitly "*have no explanation.*" (Results and Discussion, page 433, paragraph 1, *emphasis added*). The authors speculate that the observed DNA cleavage "*might* be an *artificial reaction*, occurring only in the absence of certain cofactors or additional reaction partners," or that the protein "*might* remain attached to the cleavage site," or "*might* be responsible for an activated template." [*emphasis added*]. Such speculation as to a host of different scenarios does not demonstrate that the detection of DNA nicking is predictive of transcription activity, or that identification of nicking can be used in separate methods of detecting transcription that are not even disclosed by Gansz, et al.

Further, at page 3 of the Office Action, in further support of the rejection, the Examiner lists a number of different assays methods disclosed by Gansz, et al. which purportedly measure the presence or absence of a nick in DNA, including: (1) a change in electrophoretic mobility, (2) primer extension, (3) polymerase chain reaction and amplification reaction, (4) protein binding assay, and (5) gel matrix. As outlined in Applicants' prior response and reasserted here,

none of assays described by Gansz, et al. actually teach methods of detecing transcription by detecting the presence or absence of DNA nicking, as is claimed.

Finally, at page 7 of the Office Action, the Examiner sets forth the principles that (1) disclosed examples and preferred embodiments do not constitute a teaching away from a broder disclosure or nonpreferred embodiments, citing *In re Susi*, 169 USPQ 423 (CCPA 1971), and (2) that a reference may be relied upon for all that it would reasonably suggest to one skilled in the art, including non preferred embodiments, citing *Merck & Co. v. Biocraft Laboratories*, 10 USPQ2d 1843 (Fed. Cir. 1989). Applicant does not take issue with either point of law, and has not argued otherwise, but the application of these principles to the present case is moot. Gansz, et al. does not teach any embodiment of the claimed method -- preferred, non-preferred or otherwise.

For the foregoing reasons, Applicants submit claims 1-2, 4-8, and 10-13 are patentable over Gansz, et al. under 35 U.S.C. § 102(b) and request withdrawal of the rejection.

Claim Rejections - 35 U.S.C. § 103 -

Gansz, et al. in view of Mirzabekov, et al. (U.S. Patent No. 5,851,772)

Claims 1-2 and 4-14 have been rejected over 35 U.S.C. § 103 as being obvious over Gansz, et al. in view of U.S. Patent No. 5,851,772 (Mirzabekov, et al.). Mirazabekov is relied upon for teaching DNA affixed to a biological chip.

The deficiencies of Gansz, et al. as the primary reference has been discussed above, and the combination of Gansz, et al. with the DNA chips of Mirzabekov) does nothing to alleviate

these deficiencies. Applicants therefore submit claims 1-2 and 4-14 are patentable over Gansz, et al. in view of Mirzabekov, et al. under 35 U.S.C. § 103 and request withdrawal of the rejection.

Claim Rejections - 35 U.S.C. § 103 -

Gansz, et al. in view of Hodgson, et al. (U.S. Patent No. 5,854,020)

Claims 1-8 and 10-13 have been rejected over 35 U.S.C. § 103 as being obvious over Gansz, et al. in view of Hodgson, et al. (U.S. Patent No. 5,854,020). Hodgson is relied upon for teaching a method of determining transcription initiation site by S1 nuclease activity, a transcription factor in a nuclear cell extract, and for a method of inserting the DNA template into a viral or plasmid vector.

Again, the combination of Hodgson with the primary reference Gansz, et al. does nothing to alleviate the main deficiencies of Gansz, et al. previously discussed. Applicants therefore submit claims 1-8 and 10-13 are patentable over Gansz, et al. in view of Hodgson, et al. under 35 U.S.C. § 103 and request withdrawal of the rejection.

Conclusion

In view of the foregoing, Applicant believes all claims now pending are in condition for allowance. Reconsideration and a Notice of Allowance are respectfully requested. If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at (415) 268-6524.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 506562000200.

Respectfully submitted,

Dated: August 6, 2002 By: _____

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